

Name of journal: *World Journal of Hepatology*

ESPS Manuscript NO: 12395

RE: HCC 17.10.2014 12395

Dear Editor

Thank you for your fruitful comments.

We have made the revision and we are answering point by point to the criticism.

1st reviewer: no comments

We do wish to thank the reviewer.

2nd reviewer:

Dr. Kalogeridi et al reviewed the role of radiotherapy for hepatocellular carcinoma systemically. They described the curative treatments for hepatocellular carcinoma briefly, then, focused on radiotherapy for hepatocellular carcinoma. Several problems are needed to be revised in this manuscript:

1. Too many spelling errors in this manuscript.

Answer: The paper was reviewed by a native speaking colleague (see the acknowledgment section)

2. In page 3, transplantation is considered for patients who meet the Milan criteria, not UNOS criteria.

Answer: We do agree with the reviewer. We have added now the UNOS criteria (highlighted). Also a new relevant reference has been added.

3. In page 3. The sentence "Although a cornerstone in the treatment of HCC it is limited by the shortage of organ donors." is not clear and may not be suitable.

Answer: Indeed the sentence was not clear. Please see now the corrected (highlighted)

4. Currently, artificial ascites is adopted in RFA treatment to approach the difficult areas described in the manuscript.

Answer: We do agree with the reviewer. We have added this in the revised manuscript (highlighted)

5. The results of radiotherapy should be clearly mentioned in cell studies, animal studies, phase I, phase II or phase III clinical trials because the results in different stages mean difference.

Answer: We have included now the nature of studies (see highlighted)

3rd reviewer:

The authors comprehensively reviewed the advances in radiotherapeutic treatment of HCC. In general, this is a well written review where I learned a lot. My only minor concern is to clarify the abbreviation such as KPS, EORTC, etc.

Answer: Now the abbreviations are clarified (highlighted)

This manuscript entitled "Current systemic treatment of hepatocellular carcinoma: A review of the literature" is well written. It contains all systematic treatment of HCC. I suggest the paper be accepted with minor revision. My minor concerns are as follow:

- 1) Please consider to put the introduction of mechanisms of sorafenib in front of sorafenib clinical trials.

Answer: It is now included (highlighted)

- 2) The author mentioned PD-1/PD-L1 pathway, although this has not been tested in human HCC patients. Why not mention CTLA-4 or other systematic immune therapy?

Answer: CTLA-4 is now mentioned along with a new reference (No23)

- 3) Some abbreviations such as CLIP-1, should be explained.

Answer: CLIP-1 is now explained.

We do hope that now the manuscript would suitable for publication.

Yours truly

Dr. V. Kouloulis